

INTRAVENOUS BUTORPHANOL IMPROVES CARDIOPULMONARY PARAMETERS IN GAME-RANCHED WHITE RHINOCEROSSES (*CERATOTHERIUM SIMUM*) IMMOBILIZED WITH ETORPHINE AND AZAPERONE

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ABSTRACT: We immobilized 47 white rhinoceroses (*Ceratotherium simum*) for dehorning with 1–4 mg of etorphine HCl, 10–40 mg of azaperone, and 7,500 IU of hyaluronidase, at a game ranch in South Africa in November 2012. Forty-four received butorphanol intravenously 5 min after recumbency, at the rate of 10 mg of butorphanol per 1 mg of etorphine, and three animals did not. When possible, blood gas and physiologic parameters were measured immediately before butorphanol administration and 10 min later. Statistically significant improvements were observed, with a reduction in pH, partial pressure of carbon dioxide in arterial blood, heart rate, systolic blood pressure, and diastolic blood pressure, and with an increase in arterial partial pressure of oxygen, arterial hemoglobin oxygen saturation, and respiratory rate in animals administered butorphanol. In the three animals that did not receive butorphanol, no improvement was apparent. Butorphanol given to recumbent white rhinoceroses immediately after immobilization was associated with improved blood gas values and cardiopulmonary function for at least 10 min. Studies on the sustainability of these effects are necessary.

Key words: Blood gas values, butorphanol, *Ceratotherium simum*, etorphine, hypoxemia, immobilization, white rhinoceros.

INTRODUCTION

White rhinoceroses (*Ceratotherium simum*) throughout Africa are subject to unprecedented levels of poaching. In South Africa, poaching has on average, more than doubled each year over the last 5 yr, with 668 animals killed illegally in 2012 (Biggs et al. 2013). Deterrent measures include dehorning, injecting poison into the horn, and translocation of animals to secure areas. In all cases, immobilization is used routinely, and improving the safety and efficacy of immobilization techniques has become of paramount importance.

South African white rhinoceroses are commonly immobilized with etorphine and azaperone (Burroughs et al. 2012). Etorphine, a potent opioid, acts on the μ and κ receptors. The μ receptors are primarily responsible for respiratory depression and some analgesia, and κ

receptors are primarily responsible for sedation and analgesia. Onset of effect occurs within 2–12 min of administration, and the peak effect occurs at 20–30 min (Portas 2004). However, the use of this opioid often results in adverse physiologic changes, including respiratory depression, hypoxemia, hypercapnia, acidosis, tachycardia, and hypertension (Hattingh et al. 1994; Bush et al. 2004). Azaperone, a butyrophenone neuroleptic drug, causes sedation (Plumb 2002), has minimal effects on respiration, produces peripheral vasodilation, reduces the hypertensive effects of etorphine, and may counteract the respiratory depression caused by etorphine (Portas 2004). Initial effect is seen within 15–20 min, and duration is around 6 hr. Etorphine and azaperone combinations have been used commonly for immobilization of white rhinoceros because of the low-volume, potent immobilizing effect of etorphine, and the

hypotensive effect of azaperone (Heard et al. 1992). In white rhinoceroses, hypertension secondary to increased cardiac output and increased peripheral vascular resistance is common (Raath 1999), and respiratory depression is marked (Heard et al. 1992; Kock et al. 1995; Raath 1999).

The mixed opioid agonist-antagonist nalorphine hydrobromide, used to partially antagonize the effect of etorphine to improve oxygenation during anesthesia and “walk” the rhinoceroses into crates, is no longer available on the South African market (Burroughs et al. 2012). Diprenorphine has been used, but the effect of this mixed agonist-antagonist can be unpredictable. Butorphanol tartrate, a μ -receptor antagonist and κ -receptor agonist (Branson and Cross 2001), has been used alone or in combination with azaperone to sedate or anesthetize rhinoceroses (Radcliffe et al. 2000; Portas 2004; Citino and Bush 2007; Burroughs et al. 2012). It is also frequently used in South Africa to improve respiratory depression and “walking” white and black rhinoceroses (*Diceros bicornis*) and African buffaloes (*Syncerus caffer*) (Burroughs et al. 2012; M.V.Z.L. unpubl. data). Butorphanol seems to have distinct clinical advantages over nalorphine, producing a more significant reduction in heart rate and blood pressure and an improvement in blood oxygenation in rhinoceroses (Burroughs et al. 2012).

Two studies evaluated the cardiopulmonary effects of this opioid in white rhinoceroses during etorphine and azaperone (Miller et al. 2013) and etorphine, detomidine, and azaperone immobilization (Wenger et al. 2007). Butorphanol was added to the dart with etorphine to evaluate its effect on partially negating the respiratory depressive effect of etorphine (Wenger et al. 2007; Miller et al. 2013). Adding butorphanol to the dart meant many animals remained standing (Wenger et al. 2007; Miller et al. 2013). When butorphanol was administered intravenously to recumbent, immobilized white

rhinoceroses at the rate of 20 mg per 1 mg of etorphine, median partial pressure of carbon dioxide in arterial blood (PaCO_2) and heart rate significantly decreased (Miller et al. 2013).

We further investigated the clinical effect of intravenous butorphanol, administered at the rate of 10 mg of butorphanol to 1 mg of etorphine, on the cardiopulmonary and biochemical parameters of immobilized, recumbent white rhinoceroses during dehorning in a game reserve in South Africa.

MATERIALS AND METHODS

The study subjects were game-ranched, provision-fed white rhinoceroses immobilized in November 2012 over a 2-wk period at a private game farm in the North West Province, South Africa (26°86'S, 26°66'E, 1,333 m elevation) for dehorning. Study subjects were identified from a distance by their social behavior, body size, and ear notches. Weight and age were estimated or checked with animal records. The animals were categorized into three age groups: calf (<2.5 yr), subadult (2.5–6 yr), and adult (>6 yr). The approximate weight ranged from 200 to 999 kg in calves, 1,000 to 1,600 kg in subadults, and >1,600 kg in adults.

Each rhinoceros was darted from a vehicle in the neck, shoulder, or quadriceps musculature with 4 mg of etorphine hydrochloride (Captivon, 9.8 mg/mL, Wildlife Pharmaceuticals, White River, South Africa) and 40 mg of azaperone (Stresnil, 40 mg/mL, Janssen Pharmaceutica, Johannesburg, South Africa), and 7,500 IU of hyaluronidase (Hyalase, Kyron Laboratories, Benrose, South Africa) for adult animals; 2–3 mg of etorphine and 20–30 mg of azaperone for subadults; and 1–2 mg of etorphine and 10–20 mg of azaperone for calves. Two-cubic-centimeter metal darts equipped with a 62.5-mm-length, 2.41-mm-gauge, barbed needle (Type P Pneu-darts, Pneu-dart, Inc., Williamsport, Pennsylvania, USA) were fired from a gas-powered projector (X-Caliber, Pneu-dart, Inc.). In cow and calf combinations, the cow was darted first, and, when the cow was ataxic, the calf was darted.

After darting, the animals were observed from two vehicles. For each animal, darting-to-recumbency time in seconds and animal position (lateral or sternal recumbency) were recorded. When the animal was recumbent or standing still, a blindfold was applied.

TABLE 1. Clinical description of four-level immobilization score used to assess quality of immobilization of game-ranched white rhinoceroses (*Ceratotherium simum*) in North West Province, South Africa, in November 2012 using a combination of etorphine, azaperone, and hyaluronidase.

Immobilization score level	Description
1	Recumbent—light immobilization with regular strong ear twitching, moderate muscle tremors, marked head or leg movements with legs held rigid in lateral recumbency.
2	Recumbent—moderate immobilization with occasional head movements, slight continuous ear twitching, slight continuous muscle tremors, slight continuous leg movements when in lateral recumbency.
3	Recumbent—fully relaxed immobilization, occasional ear twitching, occasional muscle tremors, occasional legs movements, and legs held in relaxed position when in lateral recumbency.
4	Recumbent—excessively deep immobilization, no ear twitching, no muscle tremors, no legs movements, and legs held in relaxed position in lateral recumbency, respiratory rate <3 breaths per minute.

Stationary, heavily sedated animals were roped down by applying a rope around a leg and pushing the body to the same side. After initial assessment, an intravenous catheter (Jelco IV Catheter radiopaque, 40 mm length, 1.27 mm gauge, Smiths Medical International Ltd., Ashford, UK) was inserted into the auricular vein, the dart was removed, the dart wound was injected with 10 mL of injectable penicillin mixture (Lentrax, 150 mg/mL procaine penicillin and 112.5 mg/mL benzathine penicillin, Merial, Midrand, South Africa), and ear plugs were inserted.

Heart rate and oxygen saturation (SpO_2) were measured using a pulse oximeter (Veterinary pulse oximeter, H100B, Edan, San Diego, California, USA) that was placed on a scarified edge of the pinna. Heart rate was also measured by auscultation with a stethoscope, and the rectal temperature was taken and recorded. Respiratory rate was measured by visual assessment of thoracic and abdominal excursions and air movement at the nares. Mucous membrane color and capillary refill time were assessed by examining the mouth, the third eyelid, or the vulval mucosa. Trends in changes in systolic and diastolic blood pressure were measured using a self-inflating human blood pressure monitor (Visacor HM40, Uebe Medical GmbH, Wertheim, Germany) attached to the tail at the level of the heart. When possible, arterial blood was collected anaerobically into 1-mL heparinized syringes from the auricular artery at 5 min (T5), 15 min (T15), and 25 min (T25) after the animal had become recumbent. Arterial partial pressure of carbon dioxide ($PaCO_2$), arterial partial pressure of oxygen (PaO_2), pH, sodium (Na^+), potassium (K^+), calcium (Ca^{2+}), glucose, and lactate were measured immediately using a

portable blood gas analyzer, the Epoc Host blood gas analyzer (Epocal, Inc., Ottawa, Ontario, Canada) using Epoc BGEM test cards. Calculated (c) hematocrit (cHct), hemoglobin (cHgb), bicarbonate ($cHCO_3^-$), base excess (BE), arterial hemoglobin oxygen saturation (SaO_2), and the concentration of total carbon dioxide (cTCO₂) were calculated simultaneously by the machine. Blood gas values were not corrected for body temperature. Body position was noted at the three time periods. The degree of immobilization during the anesthesia period was categorized using an immobilization scoring scale (Table 1).

Immediately after the first arterial blood was collected (T5), butorphanol tartrate (Butonil, 50 mg/mL, Wildlife Pharmaceuticals) was injected intravenously at the rate of 10 mg per 1 mg of etorphine into the auricular vein. In addition to the animals injected with butorphanol, some animals were used as pseudocontrols, where no butorphanol or equivalent-volume placebo was administered. The position of the animal in some instances was changed from sternal or lateral recumbency to facilitate the dehorning.

Once all procedures were complete, 20 mg of naltrexone (Trexonil, 50 mg/mL, Wildlife Pharmaceuticals) per 1 mg of etorphine was injected intravenously to antagonize the opioid component of the anesthesia, and the blindfold, intravenous catheter, and earplugs were removed. Reversal-to-standing time was recorded in seconds. During the rest of the day, recovered rhinoceroses were supervised from a distance by rangers.

Changes in physiologic and blood gas parameters before and after intravenous butorphanol were compared using a *t*-test (i.e., the difference between T5 and T15 was tested

against no change; nil difference). The potential impact of explanatory variables such as sex, age, and position on the parameter difference was explored using a *t*-test without assumption of equal variance. *P*-values were interpreted at the 0.05 significance level. Statistical analyses were conducted using STATA (Stata Statistical Software Release 12.1, Stata Corporation, College Station, Texas, USA). The complete data set is available for consultation by contacting the corresponding author.

RESULTS

In total, 47 white rhinoceroses were chemically immobilized with etorphine, azaperone, and hyaluronidase. All animals appeared healthy based on their behavior, field observations, body condition, and subsequent clinical examination. Participating animals included one female and three male calves, six male and four female subadults, and 14 male and 19 female adults. Five minutes after recumbency (T5), 44 animals were injected intravenously with butorphanol, and three animals were not given butorphanol or saline (pseudocontrol). The three pseudocontrol animals were adult males.

No mortality occurred during or following immobilization. Three animals, all females, needed to be roped down. Once recumbent, none of these animals made any attempt to stand. Median darting-to-recumbency time of animals not roped down was 405 sec (range, 140–967). In lateral recumbency, tremors of the forelimbs and hindlimbs were more noticeable, and some animals held the legs rigid (immobilization score 1, *n*=15). Animals in sternal recumbency had better muscle relaxation (immobilization score 2, *n*=7 and immobilization score 3, *n*=22). There were no immobilization scores for three animals. The median immobilization score was 3.0 (range, 1–3) across the 44 subjects injected with butorphanol.

Because of logistical problems and ambient weather conditions, physiologic data and blood gas values could not be measured systematically at T5 and 10 min later, at T15, for all animals.

The mean of the recorded physiologic data and blood gas values at T5 and T15 and subsequent mean differences for the animals injected with butorphanol are reported in Table 2. Except for oxygen saturation (SpO₂), most physiologic parameters showed significant changes before and after administration of butorphanol. Respiratory rate and rectal temperature significantly increased, while heart rate, systolic blood pressure, and diastolic blood pressure significantly decreased after the intravenous administration of butorphanol. Blood gas parameters still showed evidence of respiratory acidosis, hypoxemia, and hypercapnia after intravenous butorphanol, but there was a statistically significant improvement in pH, PaO₂, PaCO₂, and SaO₂ at T15 compared to T5. Lactate concentration stayed low, with an apparent trend toward a decrease at the second sampling point, but this was not statistically significant. Glucose and sodium concentrations increased significantly between sampling points, while the potassium concentration significantly decreased. Ca²⁺, cHct, cHCO₃⁻, cTCO₂, and base excess showed no significant change. In three pseudocontrol animals, there was a trend toward a continued abnormal derangement in PaO₂, PaCO₂, SaO₂, heart rate, respiratory rate, and systolic and diastolic blood pressure. The small number of pseudocontrols prevented statistical comparison of parameter changes with the butorphanol group. There were no significant differences between males and females and across age groups between the two sampling periods for all parameters. In the three instances where blood gas samples could be collected from animals injected with butorphanol 10 min later at T25, there was a stabilization of improvements in pH, PaO₂, PaCO₂, SaO₂, heart rates, and respiratory rates (data not shown). Recovery was uneventful, and all animals walked or ran away within 182 sec of administering the reversal agent. In two instances, immobilized animals were still

TABLE 2. Comparison of physiologic data and arterial blood gas values for immobilized game-ranched white rhinoceroses (*Ceratotherium simum*) before and after intravenous injection of butorphanol. Animals were immobilized with a combination of etorphine, azaperone, and hyaluronidase in North West Province, South Africa, in November 2012. Physiologic data and blood samples were collected before butorphanol (10 mg of butorphanol for each 1 mg of etorphine) was injected and 5 min (T5) and 15 min (T15) after recumbency. Mean blood gas and physiologic reference values previously reported from 12 healthy, standing, unrestrained, captive white rhinoceroses (Citino and Bush 2007) are added for comparison. Mean differences were compared to zero (no difference) using *t*-test to assess the impact associated with butorphanol injection, and *P*-values were interpreted at the 0.05 significance level.

Parameters ^a	Mean reference values		Mean at T5		Mean at T15		Mean difference (min-max)	SE	95% confidence interval	<i>P</i>
	(min-max) ^b	<i>n</i>	(min-max)	<i>n</i>	(min-max)	<i>n</i>				
Physiologic data										
Resp. rate (breaths/min)	19 (16-23)	42	8.5 (4-16)	40	10.7 (4-16)	39	2.2 (-4-10)	0.51	1.1-3.2	<0.001
Heart rate (beats/min)	39 (32-42)	42	118.4 (84-160)	40	73.8 (48-124)	38	-44.4 (-80- -8)	2.98	-50.46- -38.4	<0.001
Rectal temp. (C)	36.8 (36.6-37.2)	40	37.0 (35.8-38.6)	37	37.4 (35.7-38.7)	34	0.26 (-0.4-1.1)	0.07	-0.41- -0.11	<0.001
SpO ₂ (%)	-	37	97.5 (85-100)	36	98.2 (89-100)	32	-0.72 (-6-0)	0.68	-2.1-0.67	0.306
BP syst (mm Hg)	160 (146-183)	30	162.3 (80-264)	34	139.1 (62-213)	25	-22.7 (-108-77)	10.0	-43.3- -2.0	0.033
BP diastol (mm Hg)	104 (88-117)	30	103.8 (48-192)	34	80.3 (34-156)	25	-24.6 (-86-70)	41.5	-41.7- -7.41	0.007
Blood gas data										
pH	7.391 (7.346-7.431)	20	7.265 (7.163-7.335)	21	7.298 (7.234-7.366)	20	+0.033 (-0.054-0.124)	0.008	-0.05- -0.015	0.001
PaCO ₂ (mm Hg)	49.0 (44.4-53.7)	20	67.33 (44.0-91.0)	21	60.73 (51.0-70.3)	20	-6.6 (-20.9-12.3)	2.17	2.06-11.14	0.006
PaO ₂ (mm Hg)	98.3 (90.2-108.6)	20	26.71 (13.3-54.7)	21	45.03 (31.6-55.6)	20	+18.8 (4-16)	1.96	-22.9- -14.7	<0.001
Na ⁺ (mmol/L)	-	20	120.15 (103-130)	21	124.95 (116-136)	20	+4.8 (-4-19)	1.52	-8.0- -1.6	0.005
K ⁺ (mmol/L)	-	20	6.97 (4.2-11.3)	19	5.05 (3.9-6.9)	18	-1.91 (-5.9-0.3)	0.41	1.05-2.78	<0.001
Ca ²⁺ (mmol/L)	-	20	1.34 (1.02-1.55)	21	1.40 (1.22-1.63)	20	+0.06 (-0.15-0.45)	0.03	-0.13-0.01	0.089
Lactate (mmol/L)	-	20	3.1 (0.83-10.15)	21	2.9 (0.87-8.75)	20	-0.5 (-3.5-2.5)	0.27	-0.05-1.1	0.069
Glucose (mmol/L)	-	20	5.6 (3.3-8.8)	20	7.8 (4.1-12.6)	19	+2.0 (0-4.5)	0.30	-2.6- -1.3	<0.001
cHct (%)	-	20	51.8 (41-65)	19	51.2 (43-70)	18	-0.9 (-7-21)	1.52	-2.32-4.1	0.568
cHgb (g/L)	-	20	17.6 (14.0-22.1)	19	17.4 (14.5-23.8)	18	-0.37 (4-16)	2.19	-0.71-1.47	0.476
cHCO ₃ ⁻ (mmol/L)	29.3 (27.3-32.2)	20	30.5 (23.3-38.2)	21	29.5 (22.9-34.2)	20	-0.68 (-8.5-6.4)	3.60	-1.00-2.35	0.411
cTCO ₂ (mmol/L)	-	20	32.5 (24.7-41.0)	21	31.3 (24.6-36.0)	20	-0.87 (-9.1-6.7)	0.86	-0.92-2.70	0.320
cBe ECF (mmol/L)	3.5 (1.9-5.9)	20	3.5 (-4.7-10.7)	21	3.0 (-4.5-8.8)	20	-0.15 (-8.5-6.4)	3.60	-1.54-1.83	0.860
SaO ₂ (%)	97.2 (96.6-98.0)	20	38.3 (11-85.7)	21	72.6 (54.7-86.2)	20	+35.0 (-1.9-59)	3.50	-42.3- -27.7	<0.001

^a Resp. rate = respiratory rate; Rectal temp. = rectal temperature; SpO₂ = oxygen saturation; BP systol = systolic blood pressure; BP diastol = diastolic blood pressure; PaCO₂ = arterial partial pressure of carbon dioxide; PaO₂ = arterial partial pressure of oxygen; Na⁺ = sodium ions; K⁺ = potassium ions; Ca²⁺ = calcium ions; cHct = calculated hematocrit; cHgb = calculated hemoglobin; cHCO₃⁻ = calculated bicarbonate ions; cTCO₂ = concentration of total carbon dioxide; cBe ECF = calculated base excess in extracellular fluid; SaO₂ = arterial hemoglobin oxygen saturation.

^b Dashes indicate no values recorded.

slightly sedated 3 hr later, following reversal. In each case, the animals were standing and, unlike the others in their immediate group that had not been immobilized, appeared to be moving less with their head down. These two individuals were quickly aroused by noise. Neither required further reversal.

DISCUSSION

We evaluated the effect of intravenous butorphanol on the cardiopulmonary and biochemical parameters of white rhinoceroses immobilized with etorphine and azaperone. The rationale for administration is that butorphanol negates some of the respiratory depressive effects of etorphine through antagonism at the μ receptor while maintaining the sedative effects via the κ receptor.

Arterial blood gas analyses confirmed hypoxemia, hypercapnia, and respiratory acidosis 5 min after the etorphine and azaperone induction. Ten minutes after intravenous butorphanol, pH, PaO₂, PaCO₂, SaO₂, respiratory rate, heart rate, systolic blood pressure, and diastolic blood pressure significantly improved, despite levels remaining outside normal reference ranges (Citino and Bush 2007). The fact that the effect of azaperone starts later than etorphine might also explain why blood pressure was decreased at T15.

Miller et al. (2013) showed that white rhinoceroses administered butorphanol in the dart with azaperone and etorphine had a greater propensity to remain standing, thereby facilitating ventilation. Furthermore, butorphanol administered to recumbent animals, initially darted with etorphine and azaperone, produced a beneficial effect, with a significant decrease in median heart rate and PaCO₂. It was interpreted that butorphanol caused a lighter level of immobilization, allowing the animal to metabolically compensate. Although the decrease in PaCO₂ was consistent with improved ventilation, they did not observe any significant increase in

PaO₂, as seen in our study. This observation by the authors was attributed to ventilation-perfusion mismatch in the recumbent rhinoceroses and increased oxygen demand by tissues recovering from capture.

Unexpectedly, recumbent animals in our study were still more hypoxemic after butorphanol (mean PaO₂=45.03) than recumbent animals before butorphanol in the studies by Wenger et al. (2007) and Miller et al. (2013) (mean PaO₂=58.9 and 50.95, respectively). The reason for this is unknown. Maybe the provision-fed, game-ranched animals in our study were heavier and more prone to ventilation-perfusion mismatch than their counterparts found in national parks. Our study used an EPOC host blood gas analyzer, whereas the other studies used an iSTAT blood gas analyzer. However, evaluation of the analyzer revealed clinically acceptable agreement compared with a hospital blood gas analyzer, the Radiometer ABL 77 (D. Bardell et al. unpubl. data) using equine blood samples.

Improving PaO₂ in immobilized white rhinoceroses can also be achieved by providing oxygen supplementation in the field. Nasotracheal oxygen supplementation has been used effectively in rhinoceroses to increase PaO₂ and SpO₂ values (Bush et al. 2004). Oxygen supplementation had no influence on hypercapnia or metabolic acidosis. Although it can be logistically challenging in the field, oxygen supplementation during each rhinoceros immobilization remains valuable and could be used to complement the effects of intravenous butorphanol. It may also be the case that increased lactate levels and metabolic acidosis seen in the study by Miller et al. (2013), but not in our study, negated some of the effects of intravenous butorphanol on recumbent rhinos. The study by Miller et al. (2013) used twice as much butorphanol (20 mg per 1 mg of etorphine), which may have produced a dose-related effect on cardiopulmonary parameters. Wenger et al. (2007) found

no improvement in ventilation when butorphanol was added to etorphine and detomidine in the dart.

There was no substantial metabolic acidosis in our study, primarily because lactate and base excess levels were low when compared with other studies (Wenger et al. 2007; Miller et al. 2013). This could be due to the relatively quiet approach afforded by vehicles in the game-ranch animals in comparison to animals chased by a helicopter.

One limitation of this study was the absence of strict controls (animals receiving intravenous saline at the same volume of butorphanol). The limited number of controls was justified by: 1) the assumption that physiologic and blood gas parameters would not change significantly for subjects not receiving butorphanol; and 2) the fact that butorphanol has been reported to improve blood oxygenation in recumbent rhinoceroses (Burroughs et al. 2012).

Two animals showed light sedation approximately 3 hr after recovery. This sedative effect may be explained by the ongoing mild action of the azaperone, which could not be reversed, rather than renarcotization. In national parks where large carnivores exist, this may be a substantial animal safety issue and, to our knowledge, has not been recorded before.

The significant increase in blood glucose seen in the rhinos following butorphanol administration was reflected by increased glucocorticoid and epinephrine activity due to stress imposed on the animals during immobilization and is unlikely to be due to the direct effects of intravenous butorphanol. Consequently, increased serum glucose stimulates insulin, which drives potassium ions into cells, thus accounting for the significantly reduced potassium serum levels seen at T15. The activation of the renin-angiotensin-aldosterone system, due to reduced renal perfusion, leads to increased plasma aldosterone levels. This is likely to account for the increased plasma sodium levels at T15

following butorphanol administration (Mirenda and Grissom 1991).

The position of immobilized, recumbent large animals can lead to both hypoventilation and ventilation-perfusion imbalances (Hall 1971; Nyman et al. 2009) and affect physiologic and blood gas parameters (Morkel et al. 2010). In lateral recumbency, dependent lungs become atelectatic, which leads to poor ventilation, whereas the upper contralateral lung, while having opportunity for good ventilation, has poor perfusion, with the overall effect leading to ventilation-perfusion imbalance or shunted perfusion. We also investigated the impact of the animal's position on physiologic and blood gas parameters (data not shown). When comparing animals that were in sternal recumbency at T5 with animals that were in lateral recumbency, those in lateral recumbency had a significant increase in respiratory rate at T5 ($P=0.01$) and significant increase in rectal temperature at T5 ($P=0.03$) and T15 ($P=0.013$). Additionally, those animals in sternal recumbency at T5 and T15 had a marginally significant improvement ($P\sim 0.05$) in mean difference in PaO_2 and SaO_2 irrespective of the butorphanol effect. In response to the poor ventilation seen in lateral recumbency, it is suspected that animals need to increase their respiratory rate to compensate, which leads to increased muscular activity and possibly increased rectal temperature. Despite the increased respiratory rate seen in lateral recumbency, the animals still could not compensate sufficiently to improve PaO_2 and SaO_2 . The positive effect of sternal recumbency is likely due to an improved blood flow and ventilation of both sides of the lungs, leading to improved oxygenation, which was previously reported in immobilized, sternally recumbent black rhinoceroses (Morkel et al. 2010).

Maintaining the animal in sternal recumbency throughout the immobilization period, while ideal, makes dehorning more difficult. Whenever possible, it is safer for

the saw handler to have the head of the rhinoceros stabilized in lateral recumbency. As we found in this study, this may result in a deleterious effect on cardiopulmonary parameters, so it is recommended to move the rhinoceros back to sternal recumbency immediately after dehorning. This concurs with the study of Burroughs et al. (2012), who recommended that, after an animal has run some distance before going down, it should be kept in lateral recumbency to ensure good circulation to the legs, and then rolled into sternal position after 5–10 min. Consideration for further study should also include analyzing blood gas parameters when animals are positioned in their natural sleeping position where the animal lies “diagonal,” with the legs on one side flexed and the legs on the opposite side extended.

In conclusion, butorphanol administered intravenously at 10 mg of butorphanol to 1 mg of etorphine appeared to induce a direct μ antagonist effect rather than just a change in immobilization level, as previously proposed by Miller et al. (2013). This was reflected in a decrease in heart rate and an increase in respiratory rate and significant improvements in pH, PaO₂, PaCO₂, and SaO₂. Having the animal in the sternal position seemed to improve pulmonary ventilation.

Further research is required to understand how butorphanol precisely exerts its effects and the optimum intravenous dose required for etorphine-immobilized white rhinoceroses. Research to investigate the combined benefit of small amounts of butorphanol given in the darting syringe, which had an improved effect on lactate levels and pH in the study by Miller et al. (2013) and provision of butorphanol intravenously when recumbent, would also be useful.

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